CLAIMS

1. A polypeptide, which polypeptide:

(i) consists of the amino acid sequence as recited in SEQ ID NO:2 (alternative mature INSP163), SEQ ID NO: 34 (mature INSP163), SEQ ID NO: 4 (INSP163-A), SEQ ID NO: 6 (INSP163-B), SEQ ID NO: 8 (INSP163-C), SEQ ID NO: 10 (INSP163-D), SEQ ID NO: 12 (INSP163-E), and/or SEQ ID NO: 14 (INSP163-F);

(ii) is a fragment thereof which functions as a biological active polypeptide and/or has an antigenic determinant in common with the polypeptides of (i); or

(iii) is a functional equivalent of (i) or (ii).

2. A polypeptide which is a functional equivalent according to part (iii) of claim 1, characterised in that it is homologous to the amino acid sequence as recited in:

(i) SEQ ID NO:2, SEQ ID NO:34, SEQ ID NO:4, SEQ ID NO:6 and/or SEQ ID NO:8, and is a c1q and collagen domain containing polypeptide.

(ii) SEQ ID NO:10, SEQ ID NO:12 and/or SEQ ID NO: 14, and is a c1q domain containing polypeptide.

3. A fragment or functional equivalent according to part (ii) of claim 1, which has greater than 50% sequence identity with the amino acid sequence recited in SEQ ID NO: 2, SEQ ID NO:34 or with active fragments thereof, preferably greater than 60%, 70%, 80%, 90%, 95%, 98% or 99% sequence identity.

4. A fragment or functional equivalent according to part (ii) of claim 1, which has greater than 50% sequence identity with the amino acid sequence recited in SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12 and/or SEQ ID NO:14 or with active fragments thereof, preferably greater than 60%, 70%, 80%, 90%, 95%, 98% or 99% sequence identity.

5. A functional equivalent according to any one of the preceding claims, which exhibits significant structural homology with a polypeptide having the amino acid sequence given in SEQ ID NO:2, SEQ ID NO:34, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12 and/or SEQ ID NO: 14.

6. A fragment as recited in any one of the preceding claims, having an antigenic determinant in common with the polypeptide of part (i) of claim 1 which consists of 7 or more (for example, 8, 10, 12, 14, 16, 18, 20 or more) amino acid residues from the sequence of SEQ ID NO:2, SEQ ID NO:34, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12 and/or SEQ ID NO: 14.

7. A fusion protein comprising the polypeptide according to any one of the preceding claims.

8. The polypeptide of claim 7, wherein said polypeptide comprises a histidine tag.

9. The polypeptide of claim 8, whose sequence is recited in SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 36 and/or SEQ ID NO 28.

10. The polypeptide of any one of the preceding claims, wherein said polypeptide comprises a signal peptide.

11. The polypeptide of claim 10, whose sequence is recited in SEQ ID NO: 30 and/or SEQ ID NO: 32.

12. A purified nucleic acid molecule which encodes a polypeptide according to any one of the preceding claims.

13. A purified nucleic acid molecule according to claim 12, which comprises or consists of the nucleic acid sequence as recited in SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 33, SEQ ID NO: 35 and/or SEQ ID NO: 31.

14. A purified nucleic acid molecule according to claim 12 or claim 13 which consists of the nucleic acid sequence as recited in SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 33, SEQ ID NO: 35 and/or SEQ ID NO: 31, or is a redundant equivalent or fragment thereof.

15. A purified nucleic acid molecule which hybridizes under high stringency conditions with a nucleic acid molecule according any one of claims 12 to 14.

16. A vector comprising a nucleic acid molecule as recited in any one of claims 12-15.

17. A host cell transformed with a vector according to claim 16.

18. A ligand which binds specifically to a polypeptide according to any one of claims 1-11.

19. A ligand according to claim 18, which is an antibody.

20. A compound that either increases or decreases the level of expression or activity of a polypeptide according to any one of claims 1-11.

21. A compound according to claim 20 that binds to a polypeptide according to any one of claims 1-11 without inducing any of the biological effects of the polypeptide.

22. A compound according to claim 21, which is a natural or modified substrate, ligand, enzyme, receptor or structural or functional mimetic.

23. A polypeptide according to any one of claim 1-11, a nucleic acid molecule according to any one of claims 12-15, a vector according to claim 16, a host cell according to claim 17, a ligand according to claim 18 or 19, or a compound according to any one of claims 20-22, for use in therapy or diagnosis of disease.

24. A method of diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to any one of claim 1-11, or assessing the activity of a polypeptide according to any one of claim 1-11, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease.

25. A method according to claim 24 that is carried out *in vitro*.

26. A method according to claim 24 or claim 25, which comprises the steps of: (a) contacting a ligand according to claim 18 or claim 19 with a biological sample under conditions suitable for the formation of a ligand-polypeptide complex; and (b) detecting said complex.

27. A method according to claim 24 or claim 25, comprising the steps of:

(i) contacting a sample of tissue from the patient with a nucleic acid probe under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule according to any one of claims 12-15 and the probe;

(ii) contacting a control sample with said probe under the same conditions used in step a); and

(iii) detecting the presence of hybrid complexes in said samples; wherein detection of levels of the hybrid complex in the patient sample that differ from levels of the hybrid complex in the control sample is indicative of disease.

28. A method according to claim 24 or claim 25, comprising:

(i) contacting a sample of nucleic acid from tissue of the patient with a nucleic acid primer under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule according to any one of claims 12-15 and the primer;

(ii) contacting a control sample with said primer under the same conditions used in step a); and

(iii) amplifying the sampled nucleic acid; and

(iv) detecting the level of amplified nucleic acid from both patient and control samples; wherein detection of levels of the amplified nucleic acid in the patient sample that differ significantly from levels of the amplified nucleic acid in the control sample is indicative of disease.

29. A method according to claim 24 or claim 25 comprising:

(i) obtaining a tissue sample from a patient being tested for disease;

(ii) isolating a nucleic acid molecule according to any one of claims 12-15 from said tissue sample; and

(iii) diagnosing the patient for disease by detecting the presence of a mutation which is associated with disease in the nucleic acid molecule as an indication of the disease.

30. The method of claim 29, further comprising amplifying the nucleic acid molecule to form an amplified product and detecting the presence or absence of a mutation in the amplified product.

31. The method of either claim 29 or 30, wherein the presence or absence of the mutation in the patient is detected by contacting said nucleic acid molecule with a nucleic acid probe that hybridises to said nucleic acid molecule under stringent conditions to form a hybrid double-stranded molecule, the hybrid double-stranded molecule having an unhybridised

portion of the nucleic acid probe strand at any portion corresponding to a mutation associated with disease; and detecting the presence or absence of an unhybridised portion of the probe strand as an indication of the presence or absence of a disease-associated mutation.

32. A method according to any one of claims 24-31, wherein said disease is an autoimmune diseases, autoimmune inner ear disease, Labyrinthitis, Ménière disease and Ménière syndrome, Perilymphatic or labyrinthine fistula, Tinnitus, neurodegenerative diseases, amyloidosis, Alzheimer's disease, Parkinson's disease, familial dementia, inflammation (joint pain, swelling, anemia, or septic shock), infectious diseases, parasitic diseases, microbial diseases, bacterial diseases, viral diseases (HIV, HTLV, MuLV, *Streptococcus pneumoniae* and *Ascaris lumbricoides* infections), glomerulonephritis, obesity, diabetes, diabetes mellitus, Schmid metaphyseal chondrodysplasia, corneal endothelial dystrophies, posterior polymorphous corneal dystrophy (PPCD), Fuchs endothelial corneal dystrophy (FECD), atherosclerosis, scurvy, cancer, gastrointestinal stromal tumours, osteosarcoma, chondroblastoma, giant cell tumor, spondylometaphyseal dysplasia japanese type (SMD), lymphomas (Non-Hodgkin's lymphoma (NHL), follicular lymphomas, Burkitt's lymphoma, mantle cell lymphoma (MCL), multiple myeloma (MM), leukemia (chronic lymphocytic leukemia/small lymphocity lymphoma (CLL/SLL)), diffuse large cell B cell lymphoma (DLCL), B cell hyperplasia, Osteogenesis Imperfecta, Ehlers-Danlos syndrome, susceptibility to dissection of cervical arteries, aortic aneurysm, otospondylomegaepiphyseal dysplasia, hearing loss (deafness), Weissenbacher-Zweymuller syndrome, bone or skeletal disease, late-onset retinal degeneration (L-ORD), age-related macular degeneration (AMD), blindness, arthritis, rheumatoid arthritis (RA), osteoarthritis, lyme arthritis, juvenile chronic arthritis, spondyloarthropathies, Systemic lupus erythematosus (SLE), Sjögren syndrome, demyelinating diseases of the central and peripheral nervous systems such as multiple sclerosis, idiopathic demyelinating polyneuropathy or Guillain-Barre syndrome, and chronic inflammatory demyelinating polyneuropathy, myasthenia gravis, bronchitis, emphysema, renal failure (glomerulonephritis, vasculitis, nephritis or pyrlonephritis), renal neoplasms, renal cell carcinomas, renal tumour, light chain neuropathy or amyloidosis, acute or chronic immune disease associated with organ transplantation, organ transplant rejection, graft-versus-host disease, Crohn's Disease, systemic sclerosis, idiopathic inflammatory myopathies, systemic vasculitis, sarcoidosis, autoimmune hemolytic anemia, autoimmune thrombocytopenia,

thyroiditis, immune-mediated renal disease, hepatobiliary diseases such as infectious, autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis, and sclerosing cholangitis, inflammatory bowel disease, gluten-sensitive enteropathy, and Whipple's disease, autoimmune or immune-mediated skin diseases including bullous skin diseases, erythema multiforme and contact dermatitis, psoriasis, atopic dermatitis, food hypersensitivity and urticaria, immunologic diseases of the lung such as eosinophilic pneumonias, idiopathic pulmonary fibrosis and hypersensitivity pneumonitis, ulcerative colitis, inflammatory bowel disease, allergic diseases such as asthma, allergic rhinitis, sarcoidosis, female infertility, autoimmune thrombocytopenia, autoimmune thyroid disease, Hashimoto's disease, Sjogren's syndrome, ectodermal dysplasia, X-linked hypohidrotic ectodermal dysplasia (HED), inflammatory, ischemic or neoplastic diseases of the adrenal cortex, adrenal tumour, ganglioneuroblastoma, neuroblastoma, phaeochromocytomas, corstisol-producing adrenocortical adenomas, diseases linked to spinocerebellar degeneration, cerebellar diseases, olivopontocerebellar atrophy (OPCA) and/or Shy-Drager syndrome.

33. A method according to any one of claims 24 to 31, wherein said disease is a disease in which c1q domain and/or collagen domain containing proteins are implicated.

34. Use of a polypeptide according to any one of claims 1-11 as a c1q domain and/or collagen domain containing containing protein.

35. A pharmaceutical composition comprising polypeptide according to any one of claim 1-11, a nucleic acid molecule according to any one of claims 12-15, a vector according to claim 16, a host cell according to claim 17, a ligand according to claim 18 or 19, or a compound according to any one of claims 20-22.

36. A vaccine composition comprising a polypeptide according to any one of claims 1-11 or a nucleic acid molecule according to any one of claims 12-15.

37. A polypeptide according to any one of claim 1-11, a nucleic acid molecule according to any one of claims 12-15, a vector according to claim 16, a host cell according to claim 17, a ligand according to claim 18 or 19, or a compound according to any one of claims 20-21, or a pharmaceutical composition according to claim 35 for use in the manufacture of a medicament for the treatment of an autoimmune diseases, autoimmune inner ear disease, Labyrinthitis, Ménière disease and Ménière syndrome, Perilymphatic or labyrinthine fistula, Tinnitus, neurodegenerative diseases, amyloidosis, Alzheimer's disease,

Parkinson's disease, familial dementia, inflammation (joint pain, swelling, anemia, or septic shock), infectious diseases, parasitic diseases, microbial diseases, bacterial diseases, viral diseases (HIV, HTLV, MuLV, *Streptococcus pneumoniae* and *Ascaris lumbricoides* infections), glomerulonephritis, obesity, diabetes, diabetes mellitus, Schmid metaphyseal chondrodysplasia, corneal endothelial dystrophies, posterior polymorphous corneal dystrophy (PPCD), Fuchs endothelial corneal dystrophy (FECD), atherosclerosis, scurvy, cancer, gastrointestinal stromal tumours, osteosarcoma, chondroblastoma, giant cell tumor, spondylometaphyseal dysplasia japanese type (SMD), lymphomas (Non-Hodgkin's lymphoma (NHL), follicular lymphomas, Burkitt's lymphoma, mantle cell lymphoma (MCL), multiple myeloma (MM), leukemia (chronic lymphocytic leukemia/small lymphocity lymphoma (CLL/SLL)), diffuse large cell B cell lymphoma (DLCL), B cell hyperplasia, Osteogenesis Imperfecta, Ehlers-Danlos syndrome, susceptibility to dissection of cervical arteries, aortic aneurysm, otospondylomegaepiphyseal dysplasia, hearing loss (deafness), Weissenbacher-Zweymuller syndrome, bone or skeletal disease, late-onset retinal degeneration (L-ORD), age-related macular degeneration (AMD), blindness, arthritis, rheumatoid arthritis (RA), osteoarthritis, lyme arthritis, juvenile chronic arthritis, spondyloarthropathies, Systemic lupus erythematosus (SLE), Sjögren syndrome, demyelinating diseases of the central and peripheral nervous systems such as multiple sclerosis, idiopathic demyelinating polyneuropathy or Guillain-Barre syndrome, and chronic inflammatory demyelinating polyneuropathy, myasthenia gravis, bronchitis, emphysema, renal failure (glomerulonephritis, vasculitis, nephritis or pyrlonephritis), renal neoplasms, renal cell carcinomas, renal tumour, light chain neuropathy or amyloidosis, acute or chronic immune disease associated with organ transplantation, organ transplant rejection, graft-versus-host disease, Crohn's Disease, systemic sclerosis, idiopathic inflammatory myopathies, systemic vasculitis, sarcoidosis, autoimmune hemolytic anemia, autoimmune thrombocytopenia, thyroiditis, immune-mediated renal disease, hepatobiliary diseases such as infectious, autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis, and sclerosing cholangitis, inflammatory bowel disease, gluten-sensitive enteropathy, and Whipple's disease, autoimmune or immune-mediated skin diseases including bullous skin diseases, erythema multiforme and contact dermatitis, psoriasis, atopic dermatitis, food hypersensitivity and urticaria, immunologic diseases of the lung such as eosinophilic pneumonias, idiopathic pulmonary fibrosis and hypersensitivity pneumonitis, ulcerative colitis, inflammatory bowel disease, allergic diseases such as asthma, allergic rhinitis, sarcoidosis, female infertility, autoimmune

thrombocytopenia, autoimmune thyroid disease, Hashimoto's disease, Sjogren's syndrome, ectodermal dysplasia, X-linked hypohidrotic ectodermal dysplasia (HED), inflammatory, ischemic or neoplastic diseases of the adrenal cortex, adrenal tumour, ganglioneuroblastoma, neuroblastoma, phaeochromocytomas, corstisol-producing adrenocortical adenomas, diseases linked to spinocerebellar degeneration, cerebellar diseases, olivopontocerebellar atrophy (OPCA) and/or Shy-Drager syndrome.

38. A polypeptide according to any one of claims 1 to 11, a nucleic acid molecule according to any one of claims 12 to 15, a vector according to claim 16, a host cell according to claim 17, a ligand according to claim 18 or claim 19, a compound according to any one of claims 20 to 22, or a pharmaceutical composition according to claim 35, for use in the manufacture of a medicament for the treatment of a disease in which c1q domain and/or collagen domain containing proteins are implicated.

39. A method of treating a disease in a patient, comprising administering to the patient polypeptide according to any one of claims 1-11, a nucleic acid molecule according to any one of claims 12 to 15, a vector according to claim 16, a host cell according to claim 17, a ligand according to claim 18 or claim 19, a compound according to any one of claims 20 to 22, or a pharmaceutical composition according to claim 35.

40. A method according to claim 39, wherein, for diseases in which the expression of the natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an agonist.

41. A method according to claim 39, wherein, for diseases in which the expression of the natural gene or activity of the polypeptide is higher in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an antagonist.

42. A method of monitoring the therapeutic treatment of disease in a patient, comprising monitoring over a period of time the level of expression or activity of a polypeptide according to any one of claims 1-11, or the level of expression of a nucleic acid molecule according to any one of claims 12-15 in tissue from said patient, wherein altering said level of expression or activity over the period of time towards a control level is indicative of

regression of said disease.

43. A method for the identification of a compound that is effective in the treatment and/or diagnosis of disease, comprising contacting a polypeptide according to any one of claims 1-11, or a nucleic acid molecule according to any one of claims 12-15 with one or more compounds suspected of possessing binding affinity for said polypeptide or nucleic acid molecule, and selecting a compound that binds specifically to said nucleic acid molecule or polypeptide.

44. A kit useful for diagnosing disease comprising a first container containing a nucleic acid probe that hybridises under stringent conditions with a nucleic acid molecule according to any one of claims 12-15; a second container containing primers useful for amplifying said nucleic acid molecule; and instructions for using the probe and primers for facilitating the diagnosis of disease.

45. The kit of claim 44, further comprising a third container holding an agent for digesting unhybridised RNA.

46. A kit comprising an array of nucleic acid molecules, at least one of which is a nucleic acid molecule according to any one of claims 12-15.

47. A kit comprising one or more antibodies that bind to a polypeptide as recited in any one of claims 1-11; and a reagent useful for the detection of a binding reaction between said antibody and said polypeptide.

48. A transgenic or knockout non-human animal that has been transformed to express higher, lower or absent levels of a polypeptide according to any one of claims 1-11.

49. A method for screening for a compound effective to treat disease, by contacting a non-human transgenic animal according to claim 48 with a candidate compound and determining the effect of the compound on the disease of the animal.